## **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

- 1. (Canceled)
- 2. (Currently Amended) A method of treating <u>pancreatic or cervical</u> cancer in a subject in need of such treatment which comprises: <u>radiotherapy</u> a chemotherapy drug in combination with heat shock, and further comprises administering to the subject an effective amount of a matrix metalloproteinase inhibitor of the formula I

$$HO-N$$
 $R_1$ 
 $R_1$ 
 $R_1$ 

(i) wherein

A represents substituent of formula II or III;

## wherein

R represents hydrogen, lower alkyl, aryl-lower alkyl, aryl, mono- or poly-halo-lower alkyl, cycloalkyl, cycloalkyl, (oxa or thia)-cycloalkyl, [(oxa or thia)-cycloalkyl]-lower alkyl, hydroxy-lower alkyl, acyloxy-lower alkyl, lower alkoxy-lower alkyl, lower alkyl-(thio, sulfinyl or sulfonyl)-lower alkyl, (amino, mono- or di-lower alkylamino)-lower alkyl, acylamino-lower alkyl, (N-lower alkyl-piperazino or N-aryl- lower alkylpiperazino)-lower alkyl, or (morpholino, thiomorpholino, piperidino, pyrrolidino, piperidyl or N-lower alkylpiperidyl)-lower alkyl;

R<sub>3</sub> represents anyl that may be unsubstituted or substituted by R<sub>4</sub> and R<sub>5</sub>;

 $R_4$  or  $R_5$  represents independently hydrogen, lower alkyl, lower alkoxy, halogen, hydroxy, acyloxy, lower alkoxy-lower alkoxy, trifluromethyl or cyano, oxy-C2-C3-alkylene, 1- or 2-napthyl; or  $R_4$  and  $R_5$  together on adjacent carbon atoms represent lower alkylenedioxy;

n represents an integer from 1 to 5;

## wherein

 $R_6$  is  $C_{3-12}$  alkyl,  $C_{3-12}$  alkenyl,  $C_{3-7}$  (optionally hydroxy-,  $C_{1-6}$  alkoxy-, amino-, or  $C_{1-6}$  alkylamino-substituted) cycloalkyl,  $C_{5-14}$  aryl, or  $C_{5-14}$  aryl( $C_{1-6}$  alkyl), wherein aryl groups are optionally substituted by hydroxy-,  $C_{1-6}$  alkyl-,  $C_{1-6}$  alkoxy-, amino-, halo- or cyano-;

 $R_7$  is  $C_{1-10}$  (optionally hydroxy- or  $C_{1-6}$  alkoxy- amino-,  $C_{1-6}$  alkylamino-, thiol-,  $C_{1-6}$  alkylmercaptoor protected hydroxy-, amino- or thiol- substituted) alkyl,  $C_{6-14}$  (optionally hydroxy-,  $C_{6-14}$  aryloxy-, or  $C_{1-6}$  alkoxy-, amino-,  $C_{1-6}$  alkylamino-, halo-, or cyano- substituted) aryl, or indolylmethyl;

 $R_8$  is methyl, pyridyl, or a substituent of formula X-Y- wherein X is morpholino, pyridyl or aryl, and Y is  $C_{1-12}$ alkylene in which up to four of the methylene (-CH<sub>2</sub>-) units are optionally replaced with -CO-, -NH-, -SO<sub>2</sub>- or -O-;

R<sub>1</sub> is hydrogen, lower alkyl, aryl, aryl-lower alkyl, mono- or poly-halo-lower alkyl, cycloalkyl, cycloalkyl, aryl-lower alkyl-lower cycloalkyl, lower alkyl-cycloalkyl, aryl-cycloalkyl, cycloalkyl, lower alkyl-cycloalkyl, halo-lower alkyl-cycloalkyl, aryl-cycloalkyl, cycloalkyl-lower alkyl-cycloalkyl, halo-lower alkyl-cycloalkyl, hydroxy-lower alkyl, acyloxy-lower alkyl, lower alkoxy-lower alkyl, aryl-lower alkoxy-lower alkyl, (amino, mono- or di-lower alkylamino)-lower alkyl, (N-lower alkyl-piperazino or N-aryl-lower alkylpiperazino)-lower alkyl, (morpholono, thiomorpholino, piperidino, pyrrolidino, piperidyl or N-lower alkylpiperidyl)-lower alkyl, acylamino-lower alkyl, piperidyl, N-lower alkylpiperidyl or a substituent of formula iV

D-(O-(
$$CR_9H)_z$$
)<sub>m</sub>-O- $CH_2$ - Formula IV wherein  $z$  is 1, 2, 3 or 4;  $m$  is 0, 1, 2 or 3;  $each R_9$  is

independently H,  $C_{1-10}$  (optionally hydroxy-,  $C_{1-6}$  alkoxy-, amino-,  $C_{1-6}$  alkylamino-, thiol-,  $C_{1-6}$  alkylmercapto- or protected hydroxy, amino or thiol substituted) alkyl,  $C_{2-6}$  alkenyl,  $C_{6-14}$  (optionally hydroxy-,  $C_{1-6}$  alkoxy-, amino-,  $C_{1-6}$  alkylamino-, halo- or cyano- substituted) aryl, or  $C_{6-14}$  (aryl)  $C_{1-6}$  alkyl;

D is hydrogen,  $C_{1-10}$  alkyl,  $C_{6-14}$  aryl,  $C_{6-14}$  aryl( $C_{1-6}$  alkyl), ( $C_{6-14}$  aryl)carbonyl, or ( $C_{1-10}$  alkyl)carbonyl;

R<sub>2</sub> is hydrogen or lower alkyl,

(ii) or wherein

R (of formula II under (a)) and R<sub>1</sub> together with the chain to which they are attached from a 1,2,3,4-tetrahydro-isoquinoline, piperidine, oxazolidine, thiazolidine or pyrrolidine ring, each unsubstituted or substituted by lower alkyl; and

R<sub>3</sub> and R<sub>2</sub> have meaning as defined under (i);

(iii) or wherein

R<sub>1</sub> and R<sub>2</sub> together with the carbon atom to which they are attached form a ring system selected from lowercycloalkane which is unsubstituted or substituted by lower alkyl' oxa-cyclohexane, thia-cyclohexane, indane, tetralin, piperidine or piperidine substituted on nitrogen by acyl, lower alkyl, aryl-lower alkyl, (carboxy, esterified or amidated carboxy)-lower alkyl or by lower alkylsulfonyl; and

R<sub>3</sub> and R meaning as defined under (i);

or a pharmaceutically acceptable salt thereof.

- 3. (Canceled)
- 4. (Canceled)
- 5. (Currently Amended) A package comprising a matrix metalloproteinase inhibitor of formula I of claim 2\_(or pharmaceutically acceptable salt thereof) together with instructions for use in combination with <u>radiotherapy</u>

heat shock and a chemotherapy drug in the treatment of pancreatic or cervical tumor.

- 6. (canceled)
- 7. (Canceled)
- 8. (Previously Presented) A method according to claim 2, in which the matrix metalloproteinase inhibitor is N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl) amino] -3-methyl –butaneamide hydrochloride) monohydrate, or a pharmaceutically acceptable salt thereof.

- 9. (Previously presented) A method according to claim 2 in which the matrix metalloproteinase inhibitor, or a pharmacologically acceptable salt, is in the form of a enteral composition.
- 10. (Canceled)